

REMARKS

Claims 20-38 were pending in the subject application. Claims 21, 25, 27-30, 32, 33, and 35-38 have been canceled. Applicants respectfully note that independent claims 20 and 31 have been amended. Support for this amendment may be found on cancelled claims 21, 27 and 38 and page 3, lines 5-15 of the specification. This amendment does not involve any issue of new matter. Applicants respectfully request entry of the subject amendment such that claims 20, 22-24, 26, 31, and 34 will be pending.

1. Applicants acknowledge that the Examiner has made the restriction requirement final.
2. Applicants acknowledge that the Examiner has withdrawn claims 28-30, 32, and 35-37 from consideration.
3. Applicants note that the Examiner has acknowledged the claim for domestic priority.
4. Applicants acknowledge that the Examiner has accepted the drawings filed on June 16, 2000.
5. Applicants acknowledge that the Examiner has fully considered the references listed in the PTO-1449 form submitted on December 26, 2001.

Sequence Compliance

6. The Examiner contends that Applicant's previously filed Sequence Listing did not comply with the requirements, stating that not all sequences present in the specification and claims have been provided in sequence listings. In response, applicants have amended the claims and specification such that the sequences are identified by a sequence identifier. In particular, applicants have amended the specification on page 1, line 23, and in claims 20 and 31, to identify the amino acid sequence of the seven-cysteine domain of human OP-1 as amino acids 330-431 of SEQ IN NO:8. Support for this amendment may be found on page 2, lines 14-16 of

the specification. Accordingly, applicants request reconsideration and withdrawal of this ground of rejection.

Obviousness-type Double Patenting

The Examiner rejects claims 20-24, 26, 27, 31, 33, 34, and 38 under the judicially created doctrine of obviousness-type double patenting over claims 1, 4, 19, and 20 of U.S. Patent No. 6,498,142 B1 (“the ‘142 patent”). The Examiner states that the ‘142 patent teaches a method of treating a mammal at risk of chronic kidney failure with a morphogen. The Examiner further states that the patented claims are related to the instant claims as species to a genus.

The Examiner also rejects claims 20-25, 27, 31, 33, and 38 under the judicially created doctrine of obviousness-type double patenting over claims 1-5 of U.S. Patent No. 6,531,445 B1 (“the ‘445 patent”). The Examiner states that the ‘445 patent teaches a method of inducing hepatic tissue growth in the liver tissue of the mammal. The Examiner further states that the patented claims are related to the instant claims as species to a genus.

In response, applicants traverse the Examiner’s rejections. MPEP 804 section II.A.1 recites the following:

A double patenting rejection of the obviousness type is “analogous to [a failure to meet] the nonobviousness requirement of 35 U.S.C. 103” except that the patent principally underlying the double patenting rejection is not considered prior art. *In re Braithwaite* 379 F.2d 594, 154 USPQ 29 (CCPA 1967).

Therefore, any analysis employed in an obviousness-type double patenting rejection parallels the guidelines for analysis of a 35 U.S.C. 103 obviousness determination.

In addition, pursuant to MPEP 706.02(j), the following conditions must be met for an obviousness rejection: 1) the prior art references must teach or suggest all the claim limitations; 2) some motivation or suggestion, either found in the references themselves or in the knowledge

generally available to one of ordinary skill in the art, to combine or modify the references must be present; and 3) a reasonable expectation of success is required.

Furthermore, MPEP 804 section II.A.1 recites the following:

Any obviousness-type double patenting rejection should make clear:

- (A) The differences between the inventions defined by the conflicting claims – a claim in the patent compared to a claim in the application; and
- (B) The reasons why a person of ordinary skill in the art would conclude that the invention defined in the claim in issue is an obvious variation of the invention defined in the claim in the patent.

Applicants contend that the Examiner has failed to met any of the requirements as set forth in the MPEP for making a case of obviousness-type double patenting. In particular, the Examiner has failed to (a) make clear all the differences between the patented and the subject claims; (b) make clear why a person of ordinary skill in the art would conclude that the claimed invention is an obvious variation of the claimed invention; and (c) show how the cited references teach or suggest all the limitations of the instant claims. In addition to failing to meet these criteria as required by the MPEP, the Examiner has failed to clearly explain the alleged species to genus relationship between the patented and the instant claims, and in particular, to precisely define the genus and the species. Accordingly, applicants request reconsideration and withdrawal of this ground of rejection.

Claim Rejections- 35 USC §112, 1st paragraph, Enablement

Claims 20-27, 31, 33, 34 and 38 are rejected under 35 U.S.C. 112 1st paragraph because the specification allegedly does not enable the full scope of the invention. The Examiner contends that the claims encompass any morphogen, any intracellular pathway, any Smad complex, any type of cell, and any phenotype caused by any disease, and that the invention claims to cure cancer or reverse aging. The Examiner further requires applicants to amend the claims to limit the scope of the invention to those that are reasonably enabled in view of the teachings of the art and the instant specification.

In response, applicants traverse the Examiner's rejections. Applicants respectfully request that the Examiner review the language of the claims. The claims recite, in part, "method for restoring cellular phenotype in a subject's cell affected by disease, damage, or age." For example, a medial collateral ligament cell affected by advanced age may secrete reduced levels of aggrecan. Administration of OP-1 can increase the levels of aggrecan in the cell, and thus restore a cellular phenotype. Without commenting on whether or not the morphogen can treat aging, this does not necessarily mean that aging has been stopped or reversed, as the Examiner asserts, rather it means that the cellular phenotype of aggrecan expression has been restored.

Nevertheless, without conceding to the correctness of the Examiner's position but to expedite prosecution of the application, Applicants have amended claims 20 and 31 to contain the features previously recited in claims 21, 27 and 38. Furthermore, applicants have amended the claims to recite certain types of cells used by the invention, as supported, for example, by page 3, lines 5-15 of the originally filed specification. Accordingly, Applicants contend that the amended claims, and their dependent claims, are enabled by the description. Applicants respectfully request reconsideration and withdrawal of this ground of rejection.

Claim Rejections- 35 USC §112, 1st paragraph, Written Description

Claims 20-27, 31, 33 and 34 are rejected under 35 U.S.C. §112 1st paragraph because they allegedly contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention. Specifically, the Examiner objects to the claims reading on morphogens that are yet to be discovered. The Examiner contends that both a structural and a functional description of the morphogens must be recited in the claims.

Applicants note that claims 20 and 31 have been amended to recite the language of claim 38, now cancelled, which the Examiner finds to comply with the written description requirement of 35 USC §112, 1st paragraph. Amended Claims 20 and 31 recite specific morphogens and structural features for the morphogens. Accordingly, applicants request reconsideration and withdrawal of this ground of rejection.

Claim Rejections- 35 USC §112, 2nd paragraph

Claims 20-27, 31, 33, 34 and 38 are rejected under 35 U.S.C. §112 2nd paragraph as allegedly failing to particularly point out and distinctly claim the subject matter that the applicant regards as the invention. Specifically, the Examiner contends that the terms “Smad complex” in Claim 20 and 31, and “soft tissue” in Claim 33, are indefinite.

Applicants traverse this ground of rejection. As appreciated by one skilled in the art, a Smad complex is a complex comprising Smad-family proteins. The specification describes Smad complexes, for example on page 4, lines 7-11, *i.e.* “Phosphorylated Smad molecules form a heteromeric complex with at least one other specific Smad family molecule. The resulting Smad complex then translocates into and accumulates in the cell nucleus.” Page 19, lines 14-17 of the specification, further describes “smad family homodimers, heterodimers, or other homomeric or heteromeric complexes.” Furthermore, the specification describes the different Smad proteins that may be found in the complex, such as on page 3, last paragraph and page 4, first paragraph. Accordingly, the term “Smad complex” is sufficiently definite, especially when read in view of the specification.

Applicants also note that the term soft-tissue is defined on page 12, lines 11-13 of the originally filed specification as follows: “‘Soft tissue’ as used herein includes all mammalian tissue except bone and cartilage.” Accordingly, the term “soft tissue” is not indefinite. Nevertheless, Applicants have deleted the term “soft tissue” from the claims to expedite allowance of the claims. Applicants request reconsideration and withdrawal of this ground of rejection.

Claim Rejections- 35 USC §102

Claims 20-24, 27, 31, 33 and 38 are rejected under 35 U.S.C. 102 as allegedly anticipated by Rueger et al. (WO 94/03200, the “200 publication”). The Examiner states that the ‘200 publication teaches the use of morphogens to maintain neural pathways in a mammal.

According to MPEP 2131.01, “a claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described in a single prior art reference.”

Applicants note that claims 20 and 31 have been amended to recite specific cell types *i.e.* lung cells, heart cells, blood vessel cells, renal cells, stomach cells and intestinal cells. The amended claims do not recite neural cells. The ‘200 publication describes methods relating to neural cells. Accordingly, neither independent claims 20 and 31, nor their dependent claims, are anticipated by the cited reference. Applicants request reconsideration and withdrawal of this ground of rejection.

Claims 20-25, 27, 31, 33 and 38 are rejected under 35 U.S.C. 102 as allegedly anticipated by Kuberasampath et al. (WO 94/06449, the “‘449 publication”). The Examiner states that the ‘449 publication teaches the use of morphogens to maintain liver function in a mammal.

According to MPEP 2131.01, “a claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference.”

Applicants note that claims 20 and 31 have been amended to recite specific cell types *i.e.* lung cells, heart cells, blood vessel cells, renal cells, stomach cells and intestinal cells. The amended claims do not recite hepatocytes. The ‘449 publication describes methods relating to hepatocytes. Accordingly, neither independent claims 20 and 31, nor their dependent claims, are anticipated by the cited reference. Applicants request reconsideration and withdrawal of this ground of rejection.

Claim Objections-Minor Informalities

Claims 27 and 28 are objected to because they allegedly recite unelected subject matter.

Applicants have canceled Claims 27 and 28. Claims 33, 34 and 38 are objected as allegedly depending from unelected claims. Applicants have amended claims 33 and 34 to obviate this objection, and have canceled Claim 38. Accordingly, applicants request reconsideration and withdrawal of this ground of rejection.



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CONCLUSION

In view of the above, each of the presently pending claims in this application is believed to be in immediate condition for allowance. Accordingly, the Examiner is respectfully requested to pass this application to issue.

Applicant believes no fee is due with this response. However, if a fee is due, please charge our Deposit Account No. 18-1945, under Order No. JJJ-P01-520 from which the undersigned is authorized to draw.

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Respectfully submitted,

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